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(21) International Application Number: PCT/EP94/00921 (22) International Filing Date: 24 March 1994 (24.03.94) (30) Priority Data: 9306292.5 26 March 1993 (26.03.93) GB (71) Applicant (for all designated States except US): GLAXO GROUP LIMITED [GB/GB]; Glaxo House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB). (72) Inventor; and (75) Inventor/Applicant (for US only): BURT, Peter, Colin, Weston [GB/GB]; Glaxo Research and Development Limited, Park Road, Ware, Hertfordshire SG12 0DP (GB). (74) Agents: FILLER, Wendy, Anne et al.; Glaxo Holdings plc, Glaxo House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).		(81) Designated States: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: METHOD FOR FILLING AEROSOL CONTAINERS (57) Abstract A method of and an aerosol dispenser produced by purging a container which is to be filled with a substance to be dispensed and a high pressure propellant. A valve is placed on the container and prior to sealing it onto the container an amount of high pressure propellant is introduced into the container. The propellant is allowed to expand thereby forcing air out of the container through the unsealed connection between the valve and the container. The valve is then sealed onto the container.		

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Method for filling aerosol containers

The present invention relates to a method of removing air from containers which are to be filled with a substance to be dispensed and with a propellant. This removal of air is generally known as "purging" and will be so-described in this application.

The invention particularly concerns a method of purging containers which are to be filled with a suspension or solution of a substance, for example a pharmaceutical material, in a propellant which is gaseous at room temperature but is held under pressure in liquid form. Such a propellant is known as a high-pressure propellant. This type of filling method is described in UK Patent Publication No. 2236146. In this filling method, after the suspension is filled into the container, an amount of high pressure propellant without the pharmaceutical material therein is forced through the filling head, thereby cleaning the filling head and ensuring that when the filling head is lifted no suspension can escape into the atmosphere. The filling is conducted through the outlet valve of the container, because high pressure propellants are involved.

When the valves are crimped onto the containers, before filling, the containers are full of air. When the containers are filled, the air remains trapped, though obviously under pressure. The presence of air does not assist in the action of the propellant to expel the substance on activation and can also compromise the sterility of the contents if the air is not pure.

To operate the filling procedure under vacuum, thereby removing air from the containers, is not feasible. The necessary equipment would be very expensive, it is not possible to remove all air in this way, and in any case the valves are not generally designed to withstand a vacuum or partial vacuum.

Purging of air from containers containing a liquid soap solution and a volatile propellant is disclosed in US Patent 2684806. This patent discloses a purging method comprising the steps of partially filling the open containers with the soap solution and then introducing into the soap solution a gas which expands the solution into a foam until it fills the container. The valve is then sealed onto the container and the volatile propellant is introduced through the valve.

This purging system is obviously not appropriate for the filling method described in GB-A-2236146. The equivalent of the soap solution would be the

suspension of pharmaceutical material in a high pressure propellant. Unlike the soap solution, this is volatile and in any case it is highly undesirable to have the pharmaceutical material in open contact with the atmosphere. Even if high pressure propellant alone were put into the open container, this would evaporate over time; even if the container were closed quickly, movement of the container to the valve fitting station would cause air turbulence and the container would tend to entrain air into it.

According to the invention there is provided a method of purging a container which is to be filled with a substance to be dispensed and a high-pressure propellant, the purging method comprising the steps of:

- placing a valve on the container without sealing it thereon;
- introducing an amount of high-pressure propellant into the container;
- allowing the high-pressure propellant to expand and force air in the container out through the unsealed connection between the valve and the container; and
- sealing the valve onto the container.

The invention also provides an aerosol dispenser comprising a container and a valve sealed to the container, wherein the container is purged and filled by a method comprising the steps of:

- placing a valve on the container without sealing it thereon;
- introducing an amount of high-pressure propellant into the container;
- allowing the high pressure propellant to expand and force air in the container out through the unsealed connection between the valve and the container;
- sealing the valve on to the container; and
- introducing the substance to be dispensed and a further quantity of high-pressure propellant into the container through the valve after the valve has been sealed on to the container.

It has been found, surprisingly, that having the valve loose on the container allows the evaporating high-pressure propellant to expel air out around the valve while not allowing air back in. Although under-valve purging is possible, the high-pressure propellant is most advantageously filled into the container through the valve.

It should be emphasised that the advantages of the purging method of the invention do arise even for filling methods where the substance to be

dispensed is not in suspension or solution in a high-pressure propellant. In known methods, the open container can be partly filled with a substance in a low-pressure propellant (i.e. one which is liquid at room temperature). The valve can then be placed on the container and the air purged as described above, before sealing the valve and then introducing the final amount of high-pressure propellant through the valve.

An embodiment of the invention is described in more detail below, by example only, with reference to the following drawing which shows, schematically, a purging method according to the invention.

The drawing indicates three successive stations A, B and C of a purging and filling process. At station A an empty container 1 has a valve 2 simply placed thereon; the valve is not sealed onto the container, so that a limited air gap is left around the top of the container.

At station B, a filling head 3 is lowered onto the container 1 and an amount of high-pressure propellant is injected into the container. The amount may be, for example, 0.2g of liquid propellant. The filling head 3 is not described in detail since its construction will be well understood by those skilled in the art; the filling head is equivalent to a standard gassing head with an integral metering system.

The propellant drops to the bottom of the container and evaporates, displacing air out of the container. In practice the propellant will be heavier than air and so displaces the air from the bottom of the container upwards.

To prevent the pressure of the expanding propellant from tending to lift off the valve, and in order to release that pressure, the filling head should be lifted slowly off the valve, for example at a velocity of 20cm/s. After the head is lifted off the valve, it can be retracted at a higher velocity.

At station C, the valve is crimped onto the container by a crimping head 4, in a conventional fashion.

The sealed container can now be moved to a filling station at which it can be filled through the valve with a suspension of pharmaceutical substance in a high-pressure propellant followed, optionally, by propellant alone to clean the filling head.

The pharmaceutical substance can be, for example, salbutamol, beclomethasone dipropionate, salmeterol or fluticasone propionate.

The purging propellant can be the same as the filling propellant, for example 1,1,1,2-tetrafluoroethane, i.e. propellant 134a.

5 The purging method described has been found to be extremely efficient, because the valve is in place while purging occurs, loss of the propellant and entrainment of air is avoided and, in addition, the air in the valve itself is purged.

CLAIMS

1. A method of purging a container which is to be filled with a substance to be dispensed and a high-pressure propellant, the purging method comprising the steps of
- 5 placing a valve on the container without sealing it thereon;
- introducing an amount of high-pressure propellant into the container;
- 10 allowing the high-pressure propellant to expand and force air in the container out through the unsealed connection between the valve and the container; and
- 15 sealing the valve onto the container.
2. A method according to Claim 1 wherein the high pressure propellant is introduced into the container through the valve.
- 20 3. A method according to Claim 1 wherein the high pressure propellant is introduced into the container through the unsealed connection between the valve and the container.
- 25 4. A method according to any preceding claim wherein the high-pressure propellant is 1,1,1,2-tetrafluoroethane.
5. A method according to any preceding claim wherein the valve is sealed onto the container by means of a crimping head.
- 30 6. A method of filling a container comprising the steps of purging the container by means of a method according to any preceding claim and introducing the substance to be dispensed and a further quantity of high pressure propellant into the container through the valve after the valve has been sealed on to the container.
- 35

7. A method according to Claim 6 wherein the substance to be dispensed is a pharmaceutical substance.
- 5 8. A method according to Claim 7 wherein the pharmaceutical substance is salbutamol.
9. A method according to Claim 7 wherein the pharmaceutical substance is beclomethasone dipropionate.
- 10 10. A method according to Claim 7 wherein the pharmaceutical substance is salmeterol.
11. A method according to Claim 7 wherein the pharmaceutical substance is fluticasone propionate.
- 15 12. A method substantially as herein described.
13. An aerosol dispenser comprising a container and a valve sealed to the container, wherein the container is filled by a method according to any of
20 Claims 6 to 11.

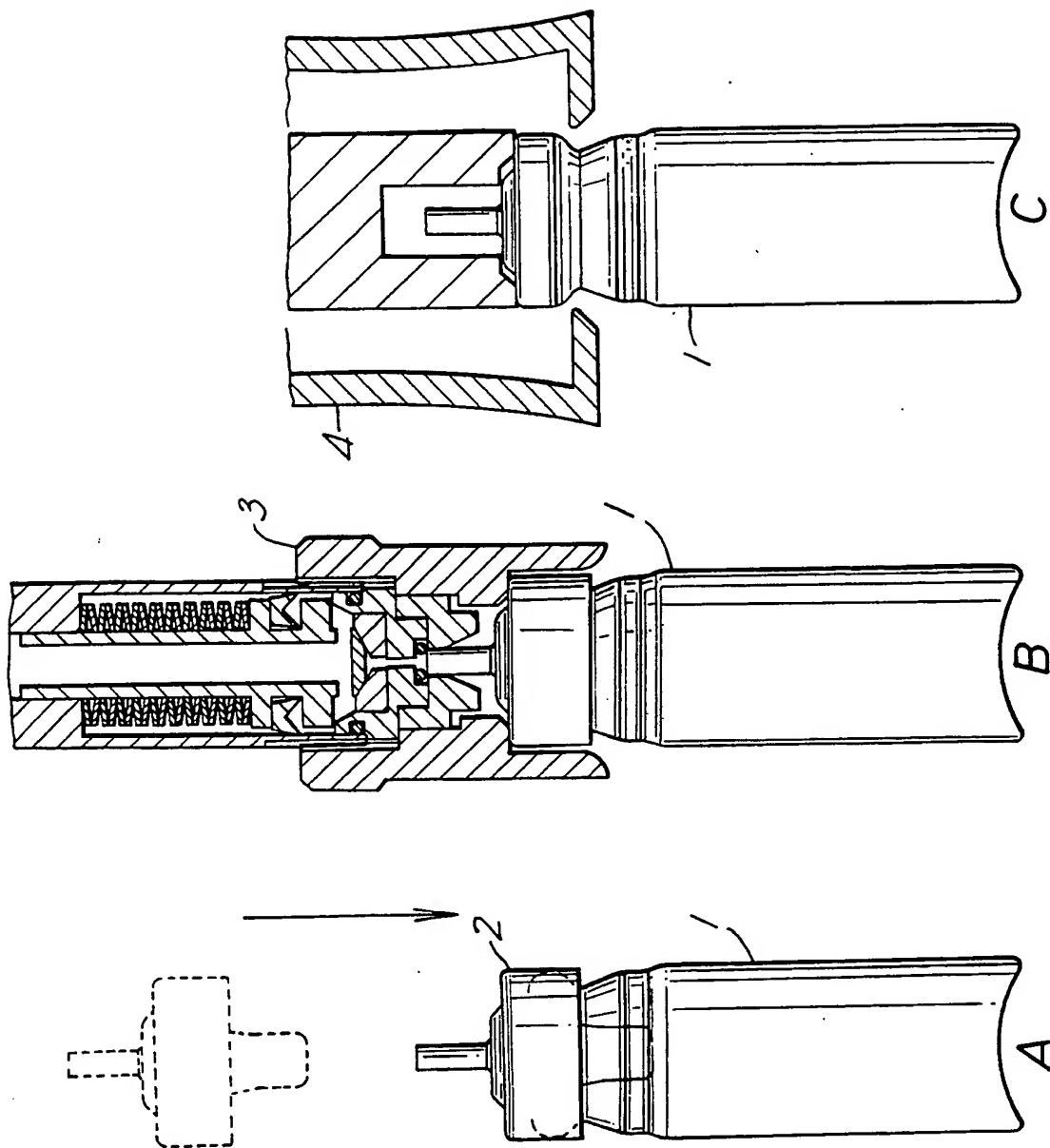


Fig. 1

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP 94/00921

A. CLASSIFICATION OF SUBJECT MATTER

IPC 5 B65B31/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 5 B65B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	GB,A,931 683 (AERATOM) 17 July 1963 see page 1, line 68 - page 2, line 13; figure 1 see page 2, line 101 - page 3, line 11 see page 3, line 32 - line 39 ---	1,6,13 2-5,7-9
Y	GB,A,2 236 146 (GLAXO) 27 March 1991 cited in the application see page 6, line 1 - line 5 see page 9, line 24 - page 10, line 15; figure 4C ---	2,4,7-9
Y	US,A,3 995 666 (VCA) 7 December 1976 see abstract ---	3
Y	GB,A,1 002 464 (NOVIMA) 25 August 1965 see page 4, line 5 - line 31; figures 1,2 -----	5

☐ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

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Date of the actual completion of the international search

14 July 1994

Date of mailing of the international search report

27. 07. 94

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP 94/ 00921

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 12
~~because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).~~
See Rule 6.2(a) PCT

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 94/00921

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB-A-931683		NONE	
GB-A-2236146	27-03-91	AU-B- 634817 AU-A- 6301190 EP-A, B 0419261 ES-T- 2043290 JP-A- 3212395	04-03-93 28-03-91 27-03-91 16-12-93 17-09-91
US-A-3995666	07-12-76	NONE	
GB-A-1002464		NONE	